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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,461	12/15/2003	Jonathan Alexander Terrett	2543-1-034	4511

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EXAMINER	
HARRIS, ALANA M	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
12/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/736,461	TERRETT, JONATHAN ALEXANDER	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05/04/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18 and 19* is/are pending in the application.

4a) Of the above claim(s) *1-12, 14-16 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments and Arguments

1. Claims 1-16, 18 and 19 are pending.

Claims 1-12, 14-16 and 18, drawn to non-elected inventions are withdrawn from examination.

Claim 13 has been amended.

Claim 17 has been cancelled.

Claim 19 has been added.

Claims 13 and 19 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

3. Applicant has filed a certified copy of the United Kingdom 011644.8 (filed June 15, 2001) application as required by 35 U.S.C. 119(b) on May 21, 2007. Consequently, the priority date afforded to the claims is June 15, 2001.

Specification

4. The disclosure is no longer objected to because it has amended the specification (see May 4, 2007 submission) to no longer contain an embedded hyperlink and/or other form of browser-executable code.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

5. The rejection of claim 13 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in light of the amendment to the claim. Claim 17 has been cancelled.

6. The rejection of claim 13 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the amendment to the claim. Claim 17 has been cancelled.

Claim Rejections - 35 USC § 102

7. The rejection of claim 13 under 35 U.S.C. 102(e) as being anticipated by US Patent Application Publication 2003/0108963 A1 (filed July 25, 2002) is withdrawn due to Applicant's newly afforded priority date of June 15, 2001.

Claim Rejections - 35 USC § 103

8. The rejection of claim 13 under 35 U.S.C. 103(a) as being unpatentable over US Patent Application Publication 2003/0108963 A1 (filed July 25, 2002), and in further view of US Patent Application Publication 2003/0108963 A1 (filed July 25, 2002) and Marin et al. (Br. J. Cancer 76(7): 923-9, 1997) is withdrawn in light of Applicant's newly afforded priority date of June 15, 2007. Claim 17 has been cancelled.

9. The rejection of claim 13 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,812,339 (effective filing date October 20, 2000) and in further view of US Patent Application Publication 2003/0108963 A1 (filed July 25, 2002) and Marin et al. (Br. J. Cancer 76(7): 923-9, 1997) is withdrawn in light of Applicant's newly afforded priority date of June 15, 2007. Claim 17 has been cancelled.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

10. Claim 19 is rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for compositions comprising antibodies or antigen binding fragments does not reasonably provide enablement for just any antibody fragments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue' not 'experimentation'. " (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of

ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims and the nature of the invention: Claim 19 is drawn to an antibody, as well as conjugated molecules including a fragment of a second antibody to be implemented in a method of treating breast cancer. The claim broadly encompasses antibody fragments such as single CDRs.

The state of the prior art and the level of predictability in the art: It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. It is expected that **all** of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl

Acad Sci USA 79:1979 (1982)). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

It is unlikely that hypervariable regions as defined by the claims, which may contain less than the full complement of CDRs from the heavy and light chain variable have the required binding function.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed inventions without undue experimentation. *In re Wright*, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support the applicants' claim to antibodies without the full complement of CDRs that retain binding specificity. All of the factors considered in the sections above, underscores the criticality of providing working examples in the specification.

Quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the Wands factors considered above, one of ordinary skill in the art would conclude that making antibodies without the full complement of CDRs would require undue experimentation in order to make the invention as claimed by the Applicants.

Applicants may obviate the instant rejection by amending the claim to include language such as antigen binding fragment of said second antibody.

Claim Rejections - 35 USC § 103

11. Claims 13 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,812,339 (effective filing date October 20, 2000) and in further view of US Patent Application Publication 2005/0159373 A1 (effective filing date March 22, 2001) and Marin et al. (Br. J. Cancer 76(7): 923-9, 1997). U.S. Patent number 6,812,339 teaches amino acid sequence 10387 which shares 99.9% sequence homology with Applicants' SEQ ID NO: 1, which is identified as a DTD polypeptide, see attached database sheet. Antibodies directed against amino acid sequences 10387 are recognized as modulators, see column 34, lines 36-41; column 36, line 59-column 37, line 2. These modulators can be administered to treat human disease, see column 35, columns 58-65. The patent does not teach the human disease is breast cancer and the antibodies are immunoconjugates.

However, the patent application publication teaches implementing an antibody, as well as fragments and immunoconjugates against the same target sequence for the treatment of breast cancer and Marin teaches the DTD enzyme is associated with breast tumors, see page 1, section 0011; page 19, sections 0198-0204 and 0209-0212; and page 20, sections 0221 and 0222. It would have been *prima facie* obvious at the time of the claimed invention to implement the teachings of the patent application, treating breast cancer in the method of administering modulators to treat human disease. And it would have been *prima facie* obvious at the time of the claimed invention to treat breast cancer given DTD is recognized as a breast cancer marker. One of ordinary skill in the art would have been motivated to combine the teachings of

all documents since the sequence homology between the target amino acid sequence and sequence 10387 is 99.9% and the patent and patent publication, both teach treating subjects with essentially the same antibodies.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
23 July 2007